We claim:

1. A method for culturing substantially purified, insulin- cells, wherein the insulin- cells differentiate to insulin+ cells, which insulin+ cells are responsive to glucose.

2. The method of claim 1, wherein the insulin+ cells are pdx1+.

3. The method of claim 1, wherein the insulin- cells are isolated from pancreas.

4. The method of claim 1, wherein the insulin- cells are isolated from duct or tubule tissue.

5. The method of claim 4, wherein the duct or tubule tissue is selected from any of pancreatic duct, hepatic duct, kidney duct, kidney tubule (e.g., proximal tubule, distal tubule), bile duct, tear duct, lactiferous duct, ejaculatory duct, seminiferous tubule, efferent duct, cystic duct, lymphatic duct, or thoracic duct.

6. The method of claim 1, wherein the insulin- cells differentiate to form islet-like structures containing insulin+ cells.

7. The method of claim 6, wherein the insulin+ cells are glucose responsive.

8. The method of claim 6, wherein the islet-like structures contain glucagon+ cells and somatostatin+ cells.

9. The method of claim 8, wherein the glucagon+ cells and the somatostatin+ cells are localized to the periphery of the islet-like structure.

10. The method of claim 1, wherein the insulin- cells are stem cells.

11. The method of claim 10, wherein the stem cells are selected from any of embryonic stem cells, fetal stem cells, or adult stem cells.

12. The method of claim 11, wherein the adult stem cells are selected from any of neural stem cells, neural crest stem cells, pancreatic stem cells, skin-derived stem cells, cardiac stem cells, liver stem cells, endothelial stem cells, hematopoietic stem cells, and mesenchymal stem cells.

13. The method of claim 11, wherein the adult stem cells are derived from an adult tissue.

14. The method of claim 13, wherein the adult tissue is selected from any of brain, spinal cord, epidermis, dermis, pancreas, liver, stomach, small intestine, large intestine, rectum, kidney, bladder, esophagus, lung, cardiac muscle, skeletal muscle, endothelium, blood, vasculature, cartilage, bone, bone marrow, uterus, tongue, or olfactory epithelium.

15. A method for differentiating substantially purified, insulin- cells to insulin+, glucose responsive cells, comprising

(a) culturing purified cells as non-adherent spheres;

(b) selecting cells by culturing in the presence of a gp130 agonist;

(c) dissociating the spheres and culturing in the presence of mitogens, wherein at least one mitogen is an FGF family member;

(d) culturing the spheres in the presence of at least two growth factors, or

growth factor agonists, wherein at least one growth factor is an FGF family member;

(e) plating the spheres on a coated substratum in high-glucose media; and

(f) culturing the spheres in media containing standard glucose.

16. The method of claim 15, wherein the gp130 agonist is selected from any of cardiotrophin-1, LIF, oncostatin M, IL-6, IL-11, ciliary neurotrophic factor, or granulocyte colony stimulating factor.

17. The method of claim 15, wherein the FGF family member of step (c) or (d) is selected from any of FGF-5, FGF-7, FGF-8, FGF-10, FGF-16, FGF-17, or FGF-18.

18. The method of claim 15, wherein the FGF family member of step (c) or (d) is selected from any of FGF-8, FGF-17, or FGF-18.

19. The method of claim 15, wherein step (c) includes a hedgehog family member selected from any of sonic hedgehog, desert hedgehog, or Indian hedgehog.

20. The method of claim 15, wherein step (c) includes an agonist of hedgehog signaling.

21. The method of any of claims claim 17-20, wherein step (c) includes heparin.

22. The method of claim 15, wherein the growth factors of (d) are family members selected from any of EGF, FGF, IGF-I, IGF-II, TGF-α, TGF-β, PDGF, VEGF, or hedgehog.

23. The method of claim 15, wherein the coated substratum of (e) comprises at least one of poly-L-ornithine, laminin, fibronectin, or superfibronectin.

24. The method of claim 23, wherein the coated substratum is superfibronectin.

25. The method of claim 15, wherein the coated substratum of (e) comprises Matrigel or a cellular feeder layer.

26. The method of claim 15, wherein the high-glucose media of (e) comprises at least 10 mM glucose.

27. The method of claim 26, wherein the high-glucose media comprises at least 11 mM glucose.

28. The method of claim 15, wherein (e) includes at least one factor selected from any of serum, PYY, HGF, or forskolin.

29. The method of claim 15, wherein (e) includes at least one cAMP elevating agent.

30. The method of claim 29, wherein at least one cAMP elevating agent is forskolin.

31. The method of claim 29, wherein the cAMP elevating agent is selected from any of CPT-cAMP, forskolin, Na-Butyrate, isobutyl methylxanthine, cholera toxin, 8-bromo-cAMP, dibutyryl-cAMP, dioctanoyl-cAMP, pertussis toxin, prostaglandins, colforsin, β-adrenergic receptor agonists, or cAMP analogs.

32. The method of claim 29, wherein at least one cAMP elevating agent is an inhibitor of cAMP phosphodiesterase.

33. The method of claim 15, wherein the standard glucose media of (f) comprises less than 7.5 mM glucose.

34. The method of claim 33, wherein the standard glucose media comprises less than 6 mM glucose.

35. The method of claim 34, wherein the standard glucose media comprises less than 5.5 mM glucose.

36. The method of claim 15, wherein the media of (f) additionally comprises at least one factor selected from any of serum, leptin, nicotinamide, malonyl CoA or exendin-4.

37. The method of claim 15, wherein the insulin- cells differentiate to form islet-like structures containing insulin+ cells.

38. The method of claim 37, wherein the islet-like structures also contain glucagon+ cells and somatostatin+ cells.

39. The method of claim 38, wherein the glucagon+ cells and the somatostatin+ cells are localized to the periphery of the islet-like structure.

40. The method of claim 15, wherein the method for differentiating substantially purified, insulin- cells to insulin+ cells includes expanding the pdx1+ cells within the non-adherent spheres.

41. A method for differentiating substantially purified, insulin- cells to insulin+, glucose responsive cells, comprising

(a) culturing purified cells as non-adherent spheres;

(b) selecting cells by culturing in serum-free media supplemented with cardiotrophin-1;

(c) dissociating the spheres and culturing in serum-free media supplemented with FGF-18 and a hedgehog polypeptide;

(d) culturing the spheres in the presence of at least two growth factors, or growth factor agonists, wherein at least one growth factor is FGF-18;

(e) plating the spheres on a coated substratum in high-glucose media; and

(f) culturing the spheres in media containing standard glucose supplemented

with nicotinamide.

42. The method of claim 41, wherein the media of (c) includes heparin.

43. The method of claim 41, wherein the growth factors of (d) are members of a growth factor family selected from any of EGF, FGF, TGF-α. TGF-β, IGF-I, IGF-II, PDGF, VEGF, or hedgehog.

44. The method of claim 41, wherein the media of (d) includes heparin.

45. The method of claim 41, wherein the coated substratum of (e) comprises at least one of poly-L-ornithine, laminin, fibronectin, or superfibronectin.

46. The method of claim 45, wherein the coated substratum of (e) comprises superfibronectin.

47. The method of claim 41, wherein the coated substratum of (e) comprises Matrigel or a cellular feeder layer.

48. A composition comprising an islet-like structure differentiated from substantially purified insulin- cells or progeny thereof.

49. A composition comprising insulin+, glucose responsive cells differentiated from substantially purified insulin- cells or progeny thereof.

50. A composition comprising an islet-like structure differentiated from substantially purified insulin- cells or progeny thereof and a pharmaceutically acceptable carrier or excipient.

51. A composition comprising insulin+, glucose responsive cells differentiated from substantially purified insulin- cells or progeny thereof and a pharmaceutically acceptable carrier or excipient.

52. A method for treating a patient with a condition characterized by impaired responsiveness to glucose, comprising administering to the patient an amount of the islet-like structures of claim 48 or 50 effective to improve glucose-responsiveness.

53. A method for treating a patient with a condition characterized by impaired responsiveness to glucose, comprising administering to the patient an amount of the insulin+, glucose responsive cells of claim 49 or 51 effective to improve glucose-responsiveness.

54. A method of increasing the number of Pdx1- cells in a non-adherent sphere of insulin- cells, wherein said Pdx1- can differentiate to Pdx1+ cells comprising

(a) culturing said insulin- cells to form non-adherent sphere; and

(b) culturing said non-adherent sphere in media comprising an FGF mitogen and a cAMP elevating agent for at least one day,

whereby following at least one day in culture in media comprising an FGF mitogen and a cAMP elevating agent the number of Pdx1- cells in said non-adherent sphere which can differentiate to Pdx1+ cells increases.

55. The method of claim 54, wherein said media is acidic media of pH 5.0-7.2.

56. The method of claim 55, wherein said media is acidic media of pH 6.9-7.1.

57. The method of claim 54, wherein said non-adherent sphere of cells is cultured in acidic media prior to addition of media comprising an FGF mitogen and a cAMP elevating agent.

58. The method of claim 57, wherein said media comprising an FGF mitogen and a cAMP elevating agent is acidic media.

59. The method of claim 57, wherein said media comprising an FGF mitogen and a cAMP elevating agent is neutral media.

60. The method of claim 54, wherein said method comprises culturing said non-adherent spheres in media comprising an FGF mitogen, a cAMP elevating agent, insulin and/or a corticosteroid.

61. The method of claim 60, wherein said FGF mitogen is selected from any of FGF-5, FGF-7, FGF-8, FGF-10, FGF-16, FGF-17, or FGF-18.

62. The method of claim 60, wherein said cAMP elevating agent is selected from any of CPT-cAMP, forskolin, Na-Butyrate, isobutyl methylxanthine, cholera toxin, 8-bromo-cAMP, dibutyryl-cAMP, dioctanoyl-cAMP, pertussis toxin, prostaglandins, colforsin, β-adrenergic receptor agonists, or cAMP analogs.

63. The method of claim 60, wherein said corticosteroid is selected from any of dexamethasone, hydrocortisone, cortisone, prednisolone, methylprednisolone, triamcinolone, or betamethasone

64. The method of claim 54, wherein said method comprises culturing said non-adherent spheres in media comprising one or more follistatin-based factors or one or more GLP-1 agonists.

65. The method of claim 54, wherein said method comprises culturing said non-adherent spheres in media comprising one or more follistatin-based factors and one or more GLP-1 agonists

66. The method of claim 64 or 65, wherein said follistatin-based factor is selected from any of a follistatin, a follistatin-related gene protein, or an inhibin.

67. The method of claim 64 or 65, wherein said GLP-1 agonist is selected from any of exendin-4, exendin-3, GLP-1, or a GLP-1 analog.

68. The method of any of claims 54, 60 or 65, further comprising differentiating said non-adherent spheres comprising Pdx-1+ cells to produce insulin+, glucose responsive cells.

69. A method of dissociating a cluster of cells, comprising culturing the cluster of cells in the presence of Protease XXIII.

70. The method of claim 69, wherein said cells are stem cells.

71. The method of claim 70, wherein said stem cells are selected from any of embryonic stem cells, fetal stem cells, or adult stem cells.

72. The method of claim 71, wherein said adult stem cells are selected from any of neural stem cells, neural crest stem cells, pancreatic stem cells, skin-derived stem cells, cardiac stem cells, liver stem cells, endothelial stem cells, hematopoietic stem cells, or mesenchymal stem cells.

73. The method of claim 71, wherein said adult stem cells are isolated from an adult tissue.

74. The method of claim 73, wherein said adult tissue is selected from any of brain, spinal cord, epidermis, dermis, pancreas, liver, stomach, small intestine, large intestine, rectum, kidney, bladder, esophagus, lung, cardiac muscle, skeletal muscle, endothelium, blood, vasculature, cartilage, bone, bone marrow, uterus, tongue, or olfactory epithelium.

75. A composition comprising substantially purified insulin+, glucose responsive cells differentiated by the method of any of claims 1, 15, 41 or 68.

76. An isolated insulin+, glucose responsive cell differentiated by the method of any of claims 1, 15, 41 or 68.

77. Use of insulin+, glucose responsive cells in the manufacture of a medicament to treat a condition in a patient, wherein said condition is characterized by an inhibition of glucose responsiveness.

78. Use of islet-like structures containing insulin+, glucose responsive cells in the manufacture of a medicament to treat a condition in a patient, wherein said condition is characterized by an inhibition of glucose responsiveness.

79. The use of claim 77 or 78, wherein said condition comprises diabetes.

80. The use of claim 77 or 78, wherein said condition comprises an injury or disease of the pancreas.

81. The use of claim 77 or 78, wherein said condition comprises an injury or disease of β-cells.